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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,129	08/24/2001	Rakesh Anand	06275-294001	9676

7590 01/30/2003

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EXAMINER	
EINSMANN, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/30/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,129	ANAND ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *4-9,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Please note that the examiner and art unit responsible for this application has changed since the issuance of the restriction requirement. The current examiner is Juliet Einsmann, and the current art unit is 1634. In order to expedite paper matching in this application, please address future correspondence accordingly.

Election/Restrictions

2. Applicant's election with traverse of Group 1, claims 1-3 in Paper No. 10 with traverse is acknowledged.

3. Since the receipt of the response, the examiner contacted applicant and agreed to rejoin one of claims 4, 5, or 10 with the elected methods, as each of these encompasses the elected methods.

4. Thus, the groups as recited in the restriction requirement (paper number 8) are modified as follows:

Group 1, claims 1-4, drawn to methods of diagnosis of a single nucleotide polymorphism and methods of predicting the clinical response to a therapeutic compound.

Group 2, claims 1-3 and 5, drawn to methods of diagnosis of a single nucleotide polymorphism and methods of assessing the predisposition of an individual to a disease.

Group 3, claims 1-3 and 10, drawn to methods of diagnosis of a single nucleotide polymorphism and methods of treating a human in need of treating.

Group 4, claim 11, drawn to methods of preparation of a medicament.

Group 5, claims 6-9, drawn to a nucleic acid with a T at position 41 in Exon 5 of the Factor X gene, allele specific oligonucleotides, and kits.

Group 6, claims 6-9, drawn to a nucleic acid with a T at position 57 in Exon 7 of the Factor X gene, allele specific oligonucleotides, and kits.

Group 7, claim 12, drawn to a computer readable medium.

These groups lack unity of invention under the PCT rules for the following reasons:

The methods and products of the instant invention are each, to some extent, concerned with the identification of or nucleic acids comprising polymorphisms in the Factor X gene. This is not a special technical feature that joins the instant claims, because this is not an advance over the prior art. Wallmark et al. (Nucleic Acids Research, Vol. 19, No. 14, page 4022) teach a method for diagnosing a polymorphism which comprises determining the sequence of the nucleic acid at a human position 57 in exon 7 of the Factor X gene. The polymorphism is a change from a C to a T. And thus, they also teach a nucleic acid that comprises the nucleic acid of EMBL ACCESSION NO. l00396 with a T at position 57. PCT Rule 13.2 states "The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes ***over the prior art***. (emphasis added)" Since the method of at least claim 1 and the nucleic acid of at least claim 6 is anticipated, the instantly claimed inventions are not joined by a special technical feature.

Furthermore, each of the methods recited in the instant claims (i.e. groups 1-4) are properly separated from one another because they are multiple processes of use. 37 CFR 1.475 states that "If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other category related thereto will be considered as the main invention of the claims." The

method 4 would require steps of predicting the response to a medicament that are not present in the other methods. The method of claim 5 requires an additional step of assessing the predisposition or susceptibility of an individual to a disease mediated by Factor X and/or Factor Xa that is not required by any of the other methods recited herein. The method of claim 10 is directed towards a method of treatment and require a treating step not required by the other methods. The methods of claim 11 are directed towards the preparation of a medicament and would thus require the steps of preparing the medicament that are not mentioned or required by the other claims. Thus, under lack of unity practice each of these methods is properly separated one from another.

The particular products that comprise groups 5-6 are not joined by a common structure with one another. In this case, the products are each separately drawn to nucleic acid molecules which comprise particular nucleotides at particular positions in a reference sequence. Each of the two separately recited products has a different particular structure from another (i.e. each claimed nucleic acid is different portion of a the Factor X gene with a particular nucleotide at a given position). These products are not joined by a special technical feature because they are each comprised of their own unique nucleic acid structure that is particular to the polymorphism of interest. The computer readable medium of group 7 is not joined to these because it is a product that is not structurally or physically joined to the nucleic acids since it is embodied as, for example, a computer disk and not a nucleic acid.

In a telephone conversation with Janis K. Fraser on 1/14/02, applicant elected, with traverse, the invention of group 3.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. Applicant's arguments set forth in the traversal of paper number 10 in light of the newly set forth restriction requirement.

Specification

6. The disclosure is objected to because of the following informalities: The specification and claims repeatedly refer to EMBL accession numbers instead of reciting sequences or sequence identifiers. This recitation is similar to the recitation of a trademark, in that the EMBL accession number does not represent a fixed disclosure of a sequence, but instead refers to a record that is constantly able to be updated and modified. Applicant should amend the specification to include the sequences which are referred to by EMBL accession numbers (and comply with the remainder of the sequence rules) and file a 132 declaration with evidence showing and stating that the newly filed sequence is identical to the sequence that was in EMBL at the time the invention was filed.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 2, 3 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10 are is indefinite over the recitation "determining the sequence of the nucleic acid of the human at position..." because it is unclear how you determine a sequence at a single position of a nucleic acid. The word "sequence" implies the determination of the nucleotide present at more than one position of a nucleic acid, yet the claims set forth that the sequence is determined at one or both of the recited positions. It is not clear how a sequence can be determined at a particular position. Amendment of the claim to recite, for example, "determination of the nucleotide present at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396" would obviate this rejection. Claims 2 and 3 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claims 1 and 10 are further indefinite over the recitation "determining the status of the human by reference to polymorphism" because it is not clear what this step is requiring. It is not clear what it means to determine the status of a human "by reference to polymorphism." Claims 2 and 3 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claim 1 and 10 are indefinite over the recitation of EMBL accession numbers (L00394 and L00396) because it is not clear as to what is encompassed by this phrase. The sequences

listed in the EMBL database are continuously updated and modified. Therefore, there is no single, fixed definition for the sequences presented as EMBL Accession No. L00396 and L00396, thus it is unclear what the claims encompass.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting and sequencing the human Factor X gene and portions thereof, does not reasonably provide enablement for methods which are limited to the detection of a polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396. Furthermore, the specification does not provide enablement for methods in which a polymorphism is diagnosed and then a Factor Xa ligand antagonist drug is administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection applies to the instant claims insofar as they might be interpreted as methods for the detection of the presence or absence of particular single nucleotide polymorphisms. It applies to claim 10 insofar as the claim implies that there would be a connection between the step of detection of the polymorphism and the administration of the Factor Xa drug. Insofar as the instant claims read generally on methods for sequencing the

Factor X gene, this rejection does not apply. The teachings of the specification (at, e.g., page 14) and of the prior art as exemplified by Leytus et al. disclose methods of detecting and sequencing the Factor X gene and portions thereof. Such methods are encompassed by the instant claims as written, and a person skilled in the art could clearly practice methods of detecting and sequencing a known gene without further guidance. However, it is unpredictable as to whether one of skill in the art could use without undue experimentation methods requiring detection of the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396 or methods for treatment which comprise detection of the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396, which methods are also encompassed by the claims.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or both of two different polymorphic sites.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an Factor X gene in a human. The methods comprise steps in which the particular nucleotide is detected at a particular position in different portions of the human Factor X gene. Claim 10 further comprises a step in which a Factor Xa ligand antagonist drug is administered in an "effective amount."

The specification teaches that Factor X involved in blood clotting and that Factor X deficiency is well documented (pages 1-2). Further, the specification provides two

polymorphisms in the Factor X gene. Both of these polymorphisms are "silent" polymorphisms, meaning that they do not alter the amino acid sequence of the encoded Factor X polypeptide. In particular, the specification teaches a polymorphic site at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396. The specification is silent with respect to the effect of these polymorphisms on the biological activity of the Factor X gene. The specification does not disclose any relationship between the presence of these polymorphisms and a change in the activity or expression of the Factor X gene or between the presence of a particular allele of this polymorphism and any particular disease state or physiological condition.

The prior art teaches a large number of polymorphisms in the Factor X gene that cause changes in the coding sequence of the Factor X gene and result in Factor X deficiencies. These all result in changes to the encoded polypeptide. For example, a review by Cooper et al. teach nineteen single base pair substitutions and deletions in the human Factor X gene that all cause changes in the encoded polypeptide (Thrombosis and Haemostasis, Vol. 78, No. 1, July 1997, pages 161-172). In addition, Wallmark et al. teach the polymorphism disclosed herein as being at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396, but Wallmark et al. do not teach the effect that this polymorphism has on the polypepetide.

There is also a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay

identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the β-globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

The level of skill in the pertinent art is quite high, i.e. generally a PhD in biochemistry, but the unpredictability in the art is higher. While the instant specification has disclosed two different polymorphisms in the Factor X gene, it remains highly unpredictable as to the biological significance of these polymorphisms. The specification merely postulates, "Other

variations in DNA sequence (polymorphisms) may not lead to Factor X deficiency, but may increase the probability of pathological conditions or affect drug response or may be linked to other polymorphisms that do so (p. 13)." Thus, the claimed method directed towards the diagnosis of polymorphisms, or treatment of disease following diagnosis of polymorphisms, for enablement of the full scope, requires the knowledge of unpredictable and potentially non-existent associations between the instantly disclosed polymorphisms and some phenotypic trait. Even if the disclosed polymorphisms are in some way associated with some disease, it is difficult (if not impossible) to know or predict from the teachings of the specification which disease or how the polymorphism is associated. That is, it is unpredictable as to whether the presence of a particular allele a polymorphism would confer a higher or lower likelihood of having the disease. In this case, the possible uses for the claimed methods are undefined, beyond the suggestion that they can be used to detect a disease associated with the a Factor X gene prior to treatment with a Factor Xa ligand antagonist drug.

The amount of direction or guidance presented in the specification with regard to how to use the instant invention is minimal. With regard to claims directed towards simple detecting the presence of the gene polymorphism, applicant speculates that "one approach is to use knowledge of polymorphisms to help identify patients most suited to therapy with particular pharmaceutical agents" However, since the effects of any given polymorphism on gene activity are highly unpredictable, it is impossible to predict from the teachings of the instant specification what identifications can be made using the instantly claimed methods. That is, the specification does not provide any guidance as to how the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in

exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396 would be associated with any pharmaceutical agent. The specification does not discuss whether this particular polymorphism will increase the likelihood of a positive or negative response to any drug. Furthermore, with regard to claim 10, which recites a method of treatment of a Factor X disease, the specification does not provide any guidance as to what disease is in fact associated with the presence or absence of the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396, other than the suggestion that these methods could be carried out for "Factor X mediated diseases." The specification further fails to provide any guidance as to the appropriate Factor Xa ligand antagonist drug to be administered after the detection of the polymorphism, or the desired effect of administration of the drug (i.e. to up or down regulate the activity of the gene, and how either of these is to be accomplished). The specification provides no guidance or working examples that teach or demonstrate the ability to use the disclosed polymorphic site as a marker for any disease in particular, or for disease in general, or how to use the disclosed polymorphism to select a proper course of treatment of a disease.

The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention, one would have to establish a relationship between the polymorphism the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396 and some physiological or disease state or some disease treatment method. Indeed, even to use the method

of claim 1 to identify patients suited for particular pharmaceutical agents, one would need to know that the polymorphism at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396 is in some way associated with response to some pharmaceutical agent. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients as well as possible hundreds of diseases or pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would be detected, in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method would be useful in disease detection and/or treatment, it is unknown as to what the outcome of such research might be and as to whether any quantity of experimentation would result in the identification of an association between the C/T polymorphism at either position and any disease or condition. Further, absent a teaching the C/T polymorphism at either position is associated with such conditions, it is further unpredictable as to whether detection of the C/T polymorphism at either position would be useful in predicting, e.g., the absence or decreased likelihood of such conditions.

Furthermore, it is noted that the practice of the invention of claim 10 requires the administration of a Factor Xa ligand antagonist drug. The specification does not define such a drug, but does teach that certain compounds are known to possess Factor Xa inhibitory properties, citing a review article and two examples (p. 1). However, the specification does not disclose a relationship between treatment with these drugs and the polymorphism at position 41

of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396. The identification of a relationship between and the elected polymorphism would be highly unpredictable, requiring an extensive amount of research and experimentation.

Thus, in light of the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of direction or working examples in the specification, and the high quantity of experimentation that would be required to practice the claimed invention, it is concluded that undue experimentation would be required to use the instantly claimed invention. Thus, with respect to claims 1-3, although the specification certainly enables one to detect the presence of the polymorphism(s) (i.e. the "make" portion of 112 1st paragraph), it would require undue experimentation in order to determine how to use the methods of claims 1-3. It would also require undue experimentation to make and use the method of claim 10. Considering all of the factors discussed herein, it is concluded that it would require undue experimentation to determine the particular disease state that can be diagnosed and treated and thus to practice the claimed invention commensurate in scope with the present claims.

Claim Rejections - 35 USC § 101

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 3 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an Factor X gene in a human and methods for treatment of disease in which the polymorphism is identified and then a drug is provided. Each of the methods comprise steps in which the particular nucleotide present is detected at a particular position in the Factor X gene as defined by particular EMBL ACCESSION numbers.

The specification teaches that the Factor X gene has been associated with a number of diseases and physiological states. Further, the specification provides two polymorphisms in the Factor X gene. In particular, the specification teaches a polymorphic site at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396. The specification suggests that the disclosed polymorphisms Factor X gene "...may not lead to Factor X deficiency, but may increase the probability of pathological conditions or affect drug response or may be linked to other polymorphisms that do so (p. 13)." Furthermore, the specification suggests that the methods can be used to detect a Factor X mediated disease.

None of these asserted utilities meet the standard of being specific, substantial, and credible. Generally, these are utilities that can be assigned to a broad class of invention, that is any method for detecting a polymorphism, thus they are not specific. Furthermore, the utilities set forth are not considered to be substantial because further experimentation would be required to reasonably confirm that the disclosed polymorphism is in fact diagnostic or prognostic of disease or in fact associated with the suitability of a particular pharmaceutical agent. The specification merely postulates that such utilities exist, but in order to practice the claimed

invention, further experimentation would be required to determine an association between the polymorphism and some physiological state or disease.

Claims 3 and 10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The utility rejection has not been applied to claims 1-2 because these claims encompass an embodiment that would have utility, namely the sequencing of the Factor X gene, which itself is known to be associated with physiological and disease states. If the claims are narrowed to exclude this embodiment, these claims may be included in the utility rejection.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wallmark et al. (Nucleic Acids Research, Vol. 19, No. 14, page 4022).

Wallmark et al. teach a method for the diagnosis of a polymorphism in a Factor X gene in a human which comprises determining the sequence of the nucleic acid of the human at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396, and determining the status of the human by reference to polymorphism in the Factor X gene. Specifically, Wallmark et al. teach a polymorphism at residue 817 of the cDNA of the

Factor X gene, which appears to be the same residue as position 57 referred to herein. The polymorphism detected by Wallmark et al. is a C→T polymorphism and is be detected by restriction length polymorphism using the enzyme NlaIV. Thus, the teachings of Wallmark et al. anticipated the instantly rejected claims.

15. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Leytus et al. (Biochemistry, 1986, 25, 5098-5102).

Leytus et al. teach a method for the diagnosis of a polymorphism in a Factor X gene in a human which comprises determining the sequence of the nucleic acid of the human at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396, and determining the status of the human by reference to polymorphism in the Factor X gene (p. 5098 and FIG. 1). Specifically, Leytus et al. teach a method for sequencing the Factor X gene (p. 5098). At least nucleotides the entire sequences taught in EMBL ACCESSION L00394 and L00396 are contained within the sequence taught by Leytus et al., thus encompassing the position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396. This reference is considered to teach the invention of claims 1 and 2 because the method contains only two method steps, one in which the sequence at position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396 is determined (i.e. which is inherently accomplished by sequencing the portion of the gene that overlaps with

position 41 of exon 5 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00394 and/or at position 57 in exon 7 of the Factor X gene as defined by the position in EMBL ACCESSION NO. L00396), and one in which the "status of the human by reference to polymorphism" is determined. Determining the sequence of the gene is considered to inherently determine the status of the human by reference to the polymorphism because by sequencing the nucleotide present at the recited positions, the status of the polymorphism is determined.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Einsmann
Examiner
Art Unit 1634

January 23, 2003

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600